AMENDMENTS TO THE SPECFICATION

Please amend the paragraph starting on line 4 of page 1 as follows:

This application: a) claims the benefit of U.S. Provisional Application No. 60/409,298, filed September 9, 2002, and U.S. Provisional Application No. 60/450,464, filed February 27, 2003 b) is a CIP of' of PCT Application No. US02/24655, filed August 2, 2002, which application claims the benefit of U.S. Provisional Application No. 60/309841, filed August 3, 2001, and U.S. Provisional Application No. 60/360061, filed February 25, 2002**, and** c) is a CIP of U.S. Non-Provisional Application No. 10/080,273, filed February 19, 2002, which application claims the benefit of U.S. Provisional Application No. 60/269,523, filed February 16, 2001~~, and d) is a CIP of U.S. Non-Provisional Application No. 09/710,059, filed November 10, 2000,~~ all of which applications are incorporated herein by reference in their entirety.

Please amend the paragraph starting on line 5 of page 109 as follows:

GST-PDZ fusion proteins (i.e. Magi1 PDZ ~~domain #1~~ **domain #2**, Syn2bp, Magi3 PDZ domain # 1, Tip1, PSD-95 PDZ domain # 2, and SAST1 were tested in pull down experiments. Briefly, 10 ug recombinant GST-PDZ proteins were incubated with 30 ul of glutathione-sepharose beads in 1 ml of buffer [50mM HEPES pH 7.4, 150mM NaCl, 10% glycerol, 0.1% Triton X-100, protease inhibitor cocktail, 1mM PMSF] for 1h at 4°C with rotation. Subsequently, cell lysates of 10^7 293 cells transiently transfected with either pMKit-HA-HPV16-E6 or pMKit-HA vector alone were incubated with the beads bound to PDZ proteins for 3h at 4°C with rotation. Beads were washed and analyzed in 12% SDS-PAGE gel electrophoresis followed by Western blotting. Membranes were probed with biotin conjugated anti-HA antibodies (clones 3F10, or 12CA5, Boehringer Mannheim) and HRP-Streptavidin (Zymed).

Please amend the paragraph starting on line 16 of page 109 as follows:

Alternatively, cell lysates from 293 cells transiently transfected with pmKit-HA, pmkit-HPV16-HA-E6 or pmKit-HA-HPV16 E6-ΔPL, were incubated with recombinant GST-Magi1-PDZ ~~domain1~~ **domain 2** protein and immobilized on glutathione-sepharose beads and bound fractions were immunoblotted with anti HA antibodies. In parallel, lysates were immunoprecipitated and detected with anti-HA antibodies.

Please amend the paragraph starting on line 23 of page 109 as follows:

G-assay PDZ-E6-PL binding studies and the determination of experimental binding affinities of the E6-PDZ interactions suggested candidate PDZ domains to be tested for the engineering of an oncogenic E6-PL-detector. In a "pull down" experiment, five different PDZ domains (Tip1; Magi1 ~~domain 1~~ **domain 2**; Sast2; Psd95 domain 2; Synaptojanin-2 binding protein) were tested for pull down of endogenous over expressed E6 from cell lysate. Lysates of cells transfected with HA-tagged E6 HPV-16 were incubated with GST-PDZ fusion protein representing the above PDZ domains bound to Sepharose beads (Figure 5). Control cell samples were transfected with HA expressing constructs. Detection with anti HA monoclonal antibody demonstrates, that E6 is selectively pulled out of cell lysates via the PDZ domain represented by the oncogenic E6-PL-detector of all five GST-PDZ proteins tested (Tip1; Magi1 ~~domain 1~~ **domain 2**; Sast2; Psd95 domain 2; Synaptojanin-2 binding protein). Results shown in Fig. 5B demonstrate that Magi 1-PDZ ~~domain 1~~ **domain 2** associates with HA-E6 but not with HA-E6ΔPL (lacking the 3 C-terminal amino acids). This method can be used to determine, whether a particular PDZ domain has the capacity of specific E6 binding. The conclusion is made, that competition by potentially PDZ binding proteins represented by the complex mixture of cell lysates and E6 for binding to PDZs can be shifted towards selective binding of E6 by appropriate choice of the specific PDZ domain that constitutes the oncogenic E6-PL detector.

Please amend the paragraph starting on line 14 of page 111 as follows:

A sandwich ELISA was conceived in two different variations. In Type 1 sandwich ELISA, E6 protein present in cell lysates in captured by E6-specific monoclonal antibody, and detection of specifically oncogenic variants occurs via the oncogenic E6-PL detector. In the type 2 ELISA set up, oncogenic E6 protein is captured via the oncogenic E6-PL detector to the solid phase and E6 detection occurs via a specific E6 antibody or another E6 binding specific agent like nucleic acid based binding compounds, chemicals binding E6, E6 binding proteins or a combination of those compounds. Cells were lysed directly on a tissue culture plate and lysates were precleared by centrifugation from insoluble components. Lysates were preincubated at 4° C with oncogenic E6-PL detector, a fusion protein of GST and Magi1 PDZ ~~domain #1~~ **domain 2**. Subsequently, lysates were loaded onto E6-specific antibody coated ELISA plates. Detection occurred via addition of HRP conjugated GST-specific antibody and addition of the HRP substrate TMB after appropriate washes between different incubation steps.

Detection signal is constituted by a colorimetric change that is quantified using absorbance measurements at 450 nm.

Please amend the paragraph starting on line 23 of page 112 as follows:

Preblock 12 well corning plates (tissue culture treated with lid, polystyrene, 22 mm well diameter) with 2 ml PBS/ 2% BSA and then rinse 3x with 2ml PBS
Spot nitrocellulose membrane with 2 ul GST-Magi1 ~~d 1~~ **domain 2** solution (88.6, 0.17 mg/ml) using 2 ul pipetman (duplicate spots in 1x1.5 cm membrane, transblot, transfer medium, supported nitrocellulose membrane, catalog no. 162-0097 (0.2 uM), Lot No. 8934). Allow to air dry for ~5-10 minutes.

Please amend the paragraph starting on line 20 of page 113 as follows:

In a sandwich type 2 setup, ~~GST-MAGI1~~ **GST-MAGI1 domain 2** oncogenic E6-PL detector was spotted on a membrane and decreasing quantities of HPV11 and HPV16 MBP-E6 fusion proteins were added for binding. Detection with E6 specific antibodies clearly demonstrated specificity of signal for oncogenic (HPV16), but not non-oncogenic E6 (HPV11). Upon longer exposure (5 minutes), HPV16 MBP-E6 quantities of 0.1 nanogram total were readily detectable (Figure 9, top).

Please amend the paragraph starting on line 1 of page 7 as follows:

An "oncogenic E6 protein binding partner" can be any molecule that specifically binds to an oncogenic E6 protein. Suitable oncogenic E6 protein binding partners include a PDZ domain (as described below), an antibody against an oncogenic E6 protein; other proteins that recognize oncogenic E6 protein (e.g., p53, E6-AP or E6-BP); DNA (i.e., cruciform DNA); and other partners such as aptamers or single chain antibodies from phage display). In some embodiments, detection of more than 1 oncogenic E6 protein (e.g., all oncogenic E6 proteins, ~~or~~ E6 proteins from HPV strains 16, 18 and 33 **or E6 proteins from HPV strains 16, 18 and 45**) is desirable, and, as such, an oncogenic E6 protein binding partner may be antibody that binds to these proteins, a mixture of antibodies that each bind to a different proteins. As is known in the art, such binding partners may be labeled to facilitate their detection. In general, binding partner bind E6 with an binding affinity of 10^{-5} M or more, e.g., 10^{-6} or more, 10^{-7} or more, 10^{-8} M or more (e.g., 10^{-9} M, 10^{-10}, 10^{-11}, etc.).